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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/718,712	11/24/2003	Kenji Sugimoto	245901US0	9928

22850 7590 10/06/2006

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EXAMINER	
DUNSTON, JENNIFER ANN	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 10/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/718,712	Applicant(s) SUGIMOTO ET AL.	
	Examiner Jennifer Dunston	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-28,31-38 and 41-44* is/are pending in the application.

4a) Of the above claim(s) *28,31-38,43 and 44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-27,41 and 42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 June 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/10/2006 has been entered.

Receipt is acknowledged of an amendment, filed 7/10/2006, in which claims 1-20, 29-30 and 39-40 were canceled; and claims 21, 43 and 44 were amended. Currently, claims 21-28, 31-38 and 41-44 are pending.

Any rejection of record in the previous office actions not addressed herein is withdrawn.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restrictions

Applicants elected Group I, and histone H3 (chromosome) and importin α (nuclear membrane) species with traverse in the reply filed on 1/28/2005. Claim 21 requires at least three fusion proteins, wherein at least one fusion protein comprises alpha-tubulin or beta tubulin. Claims 21-27 and 41-42 read on the elected species.

Claims 43 and 44 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable product claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 1/28/2005.

Claims 28 and 31-38 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 1/28/2005.

Currently, claims 21-27 and 41-42 are under consideration.

Response to Arguments - 35 USC § 112

The rejection of claims 29, 39 and 40 under 35 U.S.C. 112, second paragraph, is moot in view of Applicant's cancellation of the claims in the reply filed 7/10/2006.

Response to Arguments - 35 USC § 102

The rejection of claims 21-30 and 39-42 under 35 U.S.C. 102(b) as being anticipated by Sugimoto et al (Molecular Biology of the Cell, Vol. 13, pages 50a-51a, Abstract 282, November 1, 2002) has been withdrawn in view of Applicant's amendment to the claims in the reply filed 7/10/2006.

The rejection of claims 21-23, 25, 27-29, 39, 41 and 42 under 35 U.S.C. 102(b) as being anticipated by Gerlich et al (Nature Cell Biology, Vol. 3, pages 852-855, 2001) as evidenced by Oakley et al (Cell Structure and Function, Vol. 24, pages 365-372, 1999) has been withdrawn in view of Applicant's amendment to the claims in the reply filed 7/10/2006.

Claim Rejections - 35 USC § 103

Claims 21-23, 25, 27, 41 and 42 rejected under 35 U.S.C. 103(a) as being unpatentable over Gerlich et al (Nature Cell Biology, Vol. 3, pages 852-855, 2001, cited in a prior action; see the entire reference) in view of Rusan et al (Molecular Biology of the Cell, Vol. 12, pages 971-980, April 2001; see the entire reference). This is a new rejection.

Gerlich et al teach NRK cells (i.e. mammalian somatic cells) comprising three fusion genes: histone H2B fused to cyan fluorescent protein (H2B-CFP), lamin B receptor fused to yellow fluorescent protein (LBR-YFP), and γ-tubulin fused to red fluorescent protein (γtubulin-RFP) (e.g. page 855, Cells and DNA constructs; Figure 2). H2B-CFP, LBR-YFP, and γtubulin-RFP localize to the following cell structures: chromosome, nuclear membrane, and centrosomes, respectively (e.g. page 853, right column; Figure 2). Furthermore, Gerlich et al teach the use of the cell to study cell division (e.g. page 853, right column, first full paragraph; Figure 2).

Gerlich et al do not teach the cell comprising a polynucleotide encoding a fusion protein comprising α-tubulin and a fluorescent protein.

Rusan et al teach LLCPK-1α cells comprising a commercially available polynucleotide encoding a fusion protein comprising α-tubulin and green fluorescent protein (GFP) (e.g. page 973, Transfection and paragraph bridging columns). Microtubules containing the GFP- α-tubulin localize to and are released from the centrosome (e.g. Figure 4), and thus α-tubulin is a centrosome polypeptide. Rusan et al teach that the cells expressing GFP- α-tubulin are suitable for monitoring microtubule dynamic instability during mitosis (e.g. page 975). Rusan et al teach that it within the skill of the art to make numerous different GFP-tubulin fusion constructs (e.g. paragraph bridging pages 971-972). Furthermore, Rusan et al teach that prior to the development

of a polynucleotide encoding GFP-α-tubulin, it had been extremely difficult to directly measure microtubule dynamics in mammalian cells throughout the cell cycle and that the availability of cells expressing GFP- α-tubulin should provide a simple, easily manipulated system to examine microtubule behavior in mammalian cells (e.g. page 972, left column).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the cell comprising polynucleotides encoding three different fusion proteins of Gerlich et al to replace the γtubulin coding sequence with the α-tubulin polynucleotide taught by Rusan et al because Gerlich et al and Rusan et al teach it is within the ordinary skill in the art to make and use a polynucleotide encoding a tubulin protein fused to a fluorescent protein.

One would have been motivated to make such a modification in order to receive the expected benefit of being able to examine microtubule behavior in living mammalian cells in a simple and easily manipulated system as taught by Rusan et al and being able to visualize the chromosomes and nuclear membrane at the same time as taught by Gerlich et al. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent any evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claims 21-25, 27, 41 and 42 rejected under 35 U.S.C. 103(a) as being unpatentable over Gerlich et al (Nature Cell Biology, Vol. 3, pages 852-855, 2001, cited in a prior action; see the entire reference) in view of Rusan et al (Molecular Biology of the Cell, Vol. 12, pages 971-980, April 2001; see the entire reference) further in view of Kimura et al (The Journal of Cell

Biology, Vol. 153, No. 7, pages 1341-1353, 2001, cited in a prior action; see the entire reference. This is a new rejection.

Gerlich et al teach NRK cells (i.e. mammalian somatic cells) comprising three fusion genes: histone H2B fused to cyan fluorescent protein (H2B-CFP), lamin B receptor fused to yellow fluorescent protein (LBR-YFP), and γ-tubulin fused to red fluorescent protein (γtubulin-RFP) (e.g. page 855, Cells and DNA constructs; Figure 2). H2B-CFP, LBR-YFP, and γtubulin-RFP localize to the following cell structures: chromosome, nuclear membrane, and centrosomes, respectively (e.g. page 853, right column; Figure 2). Furthermore, Gerlich et al teach the use of the cell to study cell division (e.g. page 853, right column, first full paragraph; Figure 2).

Gerlich et al do not teach the cell comprising a polynucleotide encoding a fusion protein comprising α-tubulin and a fluorescent protein. Further, Gerlich et al do not teach the cell comprising a polynucleotide encoding a fusion protein comprising histone H3 and a fluorescent protein.

Rusan et al teach LLCPK-1α cells comprising a commercially available polynucleotide encoding a fusion protein comprising α-tubulin and green fluorescent protein (GFP) (e.g. page 973, Transfection and paragraph bridging columns). Microtubules containing the GFP- α-tubulin localize to and are released from the centrosome (e.g. Figure 4), and thus α-tubulin is a centrosome polypeptide. Rusan et al teach that the cells expressing GFP- α-tubulin are suitable for monitoring microtubule dynamic instability during mitosis (e.g. page 975). Rusan et al teach that it within the skill of the art to make numerous different GFP-tubulin fusion constructs (e.g. paragraph bridging pages 971-972). Furthermore, Rusan et al teach that prior to the development of a polynucleotide encoding GFP-α-tubulin, it had been extremely difficult to directly measure

microtubule dynamics in mammalian cells throughout the cell cycle and that the availability of cells expressing GFP- α-tubulin should provide a simple, easily manipulated system to examine microtubule behavior in mammalian cells (e.g. page 972, left column).

Kimura et al teach the replacement of histone H2B coding sequence, in a plasmid encoding a histone H2B-green fluorescent protein fusion protein, with histone H3 coding sequence such that a histone H3-green fluorescent protein (H3-GFP) fusion gene is made (e.g. page 1342, Plasmid Construction, Transfection, and Cell Fusion). Further, Kimura et al teach the transfection of the H3-GFP fusion gene into mammalian somatic cells (e.g. page 1342, Plasmid Construction, Transfection, and Cell Fusion). Moreover, Kimura et al teach that histone H3 is more stably integrated into chromatin as compared to histone H2B in that greater than 80% of histone H3 remains bound permanently to the chromosomes whereas about 53% of histone H2B remains bound permanently (e.g. Figure 7, pages 1351-1352, Transcriptional Activity of the Different Population, Concluding Remarks).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the cell comprising polynucleotides encoding three different fusion proteins of Gerlich et al to replace the γtubulin coding sequence with the α-tubulin polynucleotide taught by Rusan et al because Gerlich et al and Rusan et al teach it is within the ordinary skill in the art to make and use a polynucleotide encoding a tubulin protein fused to a fluorescent protein. Furthermore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the cell comprising fusion genes of Gerlich et al to replace the H2B coding sequence in the H2B-CFP construct taught by Gerlich et al with the H3 sequence of Kimura et al because Gerlich et al teach the use of H2B coding sequence to monitor

chromosomes and Kimura et al teach the localization of histone H3-GFP to chromosomes. Further, Kimura et al specifically teach the replacement of the H2B coding sequence with H3 coding sequence within a polynucleotide encoding a fusion protein comprising a fluorescent protein.

One would have been motivated to make such a modification in order to receive the expected benefit of being able to examine microtubule behavior in living mammalian cells in a simple and easily manipulated system as taught by Rusan et al and being able to visualize the chromosomes and nuclear membrane at the same time as taught by Gerlich et al. Further, one would have been motivated to make such a modification to include a histone H3-fluorescent protein construct in order to receive the expected benefit of more stable integration of histone H3 into chromosomes as compared to histone H2B as taught by Kimura et al. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent any evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claims 21-23, 25, 27, 41 and 42 rejected under 35 U.S.C. 103(a) as being unpatentable over Gerlich et al (Nature Cell Biology, Vol. 3, pages 852-855, 2001, cited in a prior action; see the entire reference) in view of Rusan et al (Molecular Biology of the Cell, Vol. 12, pages 971-980, April 2001; see the entire reference) further in view of Kim et al (The Journal of Biological Chemistry, Vol. 275, No. 30, pages 23139-23145, 2000, cited in a prior action; see the entire reference). This is a new rejection.

Gerlich et al teach NRK cells (i.e. mammalian somatic cells) comprising three fusion genes: histone H2B fused to cyan fluorescent protein (H2B-CFP), lamin B receptor fused to yellow fluorescent protein (LBR-YFP), and γ-tubulin fused to red fluorescent protein (γtubulin-RFP) (e.g. page 855, Cells and DNA constructs; Figure 2). H2B-CFP, LBR-YFP, and γtubulin-RFP localize to the following cell structures: chromosome, nuclear membrane, and centrosomes, respectively (e.g. page 853, right column; Figure 2). Furthermore, Gerlich et al teach the use of the cell to study cell division (e.g. page 853, right column, first full paragraph; Figure 2).

Gerlich et al do not teach the cell comprising a polynucleotide encoding a fusion protein comprising α-tubulin and a fluorescent protein. Further, Gerlich et al do not teach the cell comprising a polynucleotide encoding a fusion protein comprising importin α and a fluorescent protein.

Rusan et al teach LLCPK-1α cells comprising a commercially available polynucleotide encoding a fusion protein comprising α-tubulin and green fluorescent protein (GFP) (e.g. page 973, Transfection and paragraph bridging columns). Microtubules containing the GFP- α-tubulin localize to and are released from the centrosome (e.g. Figure 4), and thus α-tubulin is a centrosome polypeptide. Rusan et al teach that the cells expressing GFP- α-tubulin are suitable for monitoring microtubule dynamic instability during mitosis (e.g. page 975). Rusan et al teach that it within the skill of the art to make numerous different GFP-tubulin fusion constructs (e.g. paragraph bridging pages 971-972). Furthermore, Rusan et al teach that prior to the development of a polynucleotide encoding GFP-α-tubulin, it had been extremely difficult to directly measure microtubule dynamics in mammalian cells throughout the cell cycle and that the availability of

cells expressing GFP- α-tubulin should provide a simple, easily manipulated system to examine microtubule behavior in mammalian cells (e.g. page 972, left column).

Kim et al teach a polynucleotide encoding a fusion protein comprising importin α and green fluorescent protein (GFP) (e.g. page 23140, Plasmid Construction and Expression of Fusion Proteins). Further, Kim et al teach the transfection of mammalian somatic CHO-K1 cells, where the Importin α-GFP fusion protein localized to the nucleus (e.g. Figure 4).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the cell comprising polynucleotides encoding three different fusion proteins of Gerlich et al to replace the γtubulin coding sequence with the α-tubulin polynucleotide taught by Rusan et al because Gerlich et al and Rusan et al teach it is within the ordinary skill in the art to make and use a polynucleotide encoding a tubulin protein fused to a fluorescent protein. Further, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the cell of Gerlich et al to replace the LBR sequence in the LBR-YFP fusion polynucleotide with the importin α sequence taught by Kim et al because Gerlich et al teach it is within the skill of the art to make cells comprising fluorescent fusion proteins to monitor the nucleus/nuclear membrane during cell division and Kim et al teach the localization of Importin α-GFP to the nucleus, a cellular structure involved in cell division.

One would have been motivated to make such a modification in order to receive the expected benefit of being able to examine microtubule behavior in living mammalian cells in a simple and easily manipulated system as taught by Rusan et al and being able to visualize the chromosomes and nuclear membrane at the same time as taught by Gerlich et al. Further, one would have been motivated to include an importin α-fluorescent protein construct to receive the

expected benefit of being able to monitor the nucleus of the cell as taught by Kim et al and expand the repertoire of proteins available for monitoring the nuclear structure. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent any evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claims 21-27 and 41-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sugimoto et al (Molecular Biology of the Cell, Vol. 13, pages 50a-51a, Abstract 282, November 1, 2002, cited in a prior action; see the entire abstract) in view of Rusan et al (Molecular Biology of the Cell, Vol. 12, pages 971-980, April 2001; see the entire reference). This is a new rejection.

Sugimoto et al teach a human stable cell line comprising polynucleotides encoding three fusion proteins: histone H3 fused to cyan fluorescent protein (CFP-histone H3), importin α fused to red fluorescent protein (DsRed-importinα), and Aurora-A fused to green fluorescent protein (GFP-Aurora-A) (paragraph bridging pages 50a-51a). CFP-histone H3, DsRed-importinα, and EGFP-Aurora-A localize to the following cell structures: chromosome, nuclear membrane, and centrosome, respectively, and can be used to monitor cell division (paragraph bridging pages 50a-51a).

Sugimoto et al do not teach the cell comprising a polynucleotide encoding a fusion protein comprising α-tubulin and a fluorescent protein.

Rusan et al teach LLCPK-1α cells comprising a commercially available polynucleotide encoding a fusion protein comprising α-tubulin and green fluorescent protein (GFP) (e.g. page

973, Transfection and paragraph bridging columns). Microtubules containing the GFP- α-tubulin localize to and are released from the centrosome (e.g. Figure 4), and thus α-tubulin is a centrosome polypeptide. Rusan et al teach that the cells expressing GFP- α-tubulin are suitable for monitoring microtubule dynamic instability during mitosis (e.g. page 975). Rusan et al teach that it within the skill of the art to make numerous different GFP-tubulin fusion constructs (e.g. paragraph bridging pages 971-972). Furthermore, Rusan et al teach that prior to the development of a polynucleotide encoding GFP-α-tubulin, it had been extremely difficult to directly measure microtubule dynamics in mammalian cells throughout the cell cycle and that the availability of cells expressing GFP- α-tubulin should provide a simple, easily manipulated system to examine microtubule behavior in mammalian cells (e.g. page 972, left column).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the cell comprising polynucleotides encoding three different fusion proteins of Sugimoto et al to replace the polynucleotide encoding Aurora-A-GFP with the polynucleotide encoding GFP-α-tubulin of Rusan et al because Sugimoto et al and Rusan et al teach it is within the ordinary skill in the art to make and use a polynucleotide encoding a cell structure protein fused to a green fluorescent protein.

One would have been motivated to make such a modification in order to receive the expected benefit of being able to examine microtubule behavior in living mammalian cells in a simple and easily manipulated system as taught by Rusan et al and being able to visualize the chromosomes and nuclear membrane at the same time as taught by Sugimoto et al. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent

any evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Response to Arguments - 35 USC § 103

The rejection of claims 24 and 26 under 35 U.S.C. 103(a) as being unpatentable over Gerlich et al (Nature Cell Biology, Vol. 3, pages 852-855, 2001) in view of Kimura et al (The Journal of Cell Biology, Vol. 153, No. 7, pages 1341-1353, 2001) further in view of Kim et al (The Journal of Biological Chemistry, Vol. 275, No. 30, pages 23139-23145, 2000), as evidenced by Oakley et al (Cell Structure and Function, Vol. 24, pages 365-372, 1999) has been withdrawn in view of Applicant's amendment to the claims in the reply filed 7/10/2006.

Relevant Prior Art

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

Ravkin et al (US Patent Application Publication No. 2003/0059764). Ravkin et al teach multiplexed analysis of spindle defects using a cell that contains GFP-tubulin (alpha or beta) fusion proteins, a microtubule organizing center (MTOC) label such as a gamma-tubulin label, and a DNA/chromosome label such as a histone label (e.g. paragraphs [0312]-[0313]).

Clonetch Catalog 2000, pages 210-211. The Clontech catalog discloses commercially available plasmids encoding fluorescent proteins fused to proteins that are markers of actin filaments, microtubules, endoplasmic reticulum, golgi apparatus, membrane, mitochondria and nucleus.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dunston whose telephone number is 571-272-2916. The examiner can normally be reached on M-F, 9 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jennifer Dunston, Ph.D.
Examiner
Art Unit 1636

jad

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